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They Came from the Dust: Indoor Endocrine Disruptors and Thyroid-Hormone Binding

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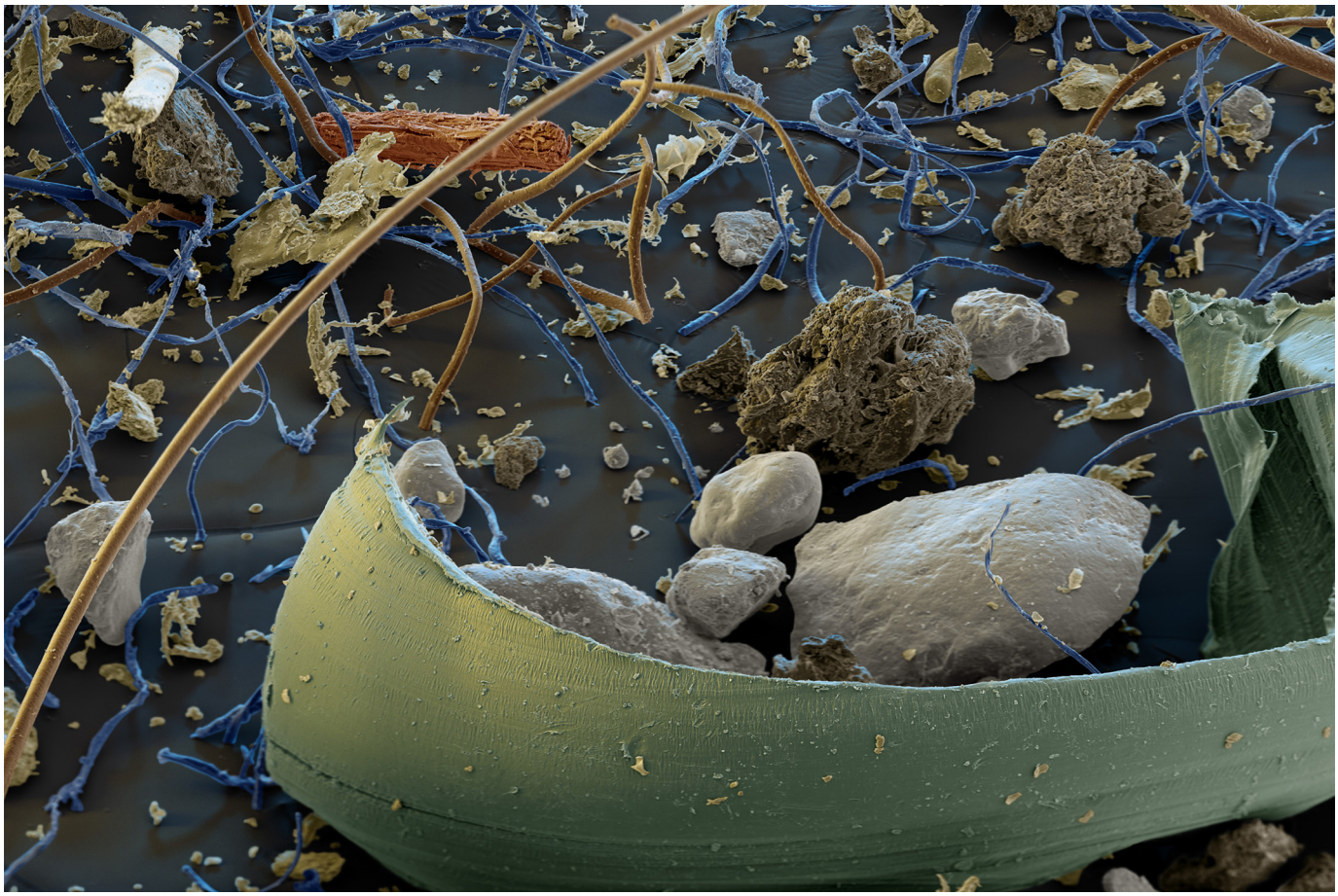
House dust can contain complex mixtures of endocrine-disrupting compounds (EDCs),[1,2] which can interfere with the synthesis, transport, or actions of thyroid hormones, including thyroxine (T_4).[2,3] In a recent study published in *Environmental Health Perspectives*,[1] researchers assessed the ability of house dust contaminant mixtures to interfere with T_4 binding to transthyretin (TTR), a protein involved in transporting the hormone to target tissues. Extrapolating *in vitro* results to *in vivo* binding potencies, the researchers estimated a slight but potentially meaningful decrease in T_4 binding due to contaminant mixtures.

In response to signals from the hypothalamus passed along by the pituitary gland, the thyroid produces T_4—which is a prohormone, or precursor hormone—and a smaller amount of the active hormone triiodothyronine (T_3). These hormones interact with receptors in target tissues to trigger a cascade of reactions leading to a biological response. Negative feedback loops serve to keep the thyroid system properly calibrated. Such control is particularly critical during pregnancy because the developing fetus depends on maternal thyroid hormones for normal development.[4]

Previous research has shown that people can be exposed to EDCs in house dust.[2] "People spend the majority of their time indoors, and I think we have this sense that we're more protected from these contaminant exposures indoors than we are outdoors," says Heather Stapleton, an associate professor at the Nicholas School of the Environment, Duke University, who was not involved in the new study. "But that's actually not the case, because if you analyze house dust for contaminants, there [are] so many different chemicals in there," she says. These dust-borne EDCs can enter the body through inhalation, ingestion, or dermal absorption.[2]

The current study was part of a larger Swedish project on EDCs known as Mixture aSSessments of EDCs (MiSEE; https://www.aces.su.se/misse/). The researchers selected 25 compounds that are known to bind to TTR and have previously been identified in house dust, maternal serum, and infant serum or cord blood. They created mixtures representing the median concentrations of the compounds identified in each of these media. They also produced an extract from Standard Reference Material (SRM) 2585, a stock mixture of organic contaminants in a dust matrix.



Scanning electron micrograph of house dust, magnification 50:1. This sample contains fragments of plastic (green shavings), textile fibers (blue strands), particles of dirt (dark brown) and sand (light gray), hairs (light brown), and an orange splinter of wood. These and other dust constituents can carry EDCs from sources such as electronics, treated fabrics, building materials, and the outdoors.[2] Image: © Eye of Science/Science Source.

The researchers used *in vitro* assays to determine the extent to which individual compounds, the reconstituted mixtures, and the SRM2585-based extract altered T_4 binding to TTR. These assays revealed that the measured overall T_4-displacing effect of each mixture was well predicted by adding up the contributions of the constituents relative to their individual TTR-binding potencies and concentrations.

Next, they extrapolated this information to estimate the inhibition that might occur *in vivo*, an even more complicated setting due to the presence of other T_4 carriers. Overall, the contaminant mixtures led to an estimated 1.3–1.5% inhibition of T_4 binding to TTR *in vivo*. Given that TTR binding accounts for only 3–4% of the total T_4 in pregnant women and infants, the absolute amount of displaced T_4 was quite small. Nevertheless, TTR has an outsized role in the precise delivery of T_4 at target sites. For women who already have compromised thyroid status (e.g., hypothyroxinemia or hypothyroidism), any disruption could be relevant for the developing fetus.

"TTR is very critical because that's the one that's ultimately delivering the thyroid hormone to the tissues, and if you mess around with TTR, then you may still have a problem," says study leader Timo Hamers, an associate professor in the Department of Environment and Health at Vrije Universiteit Amsterdam. Hamers notes that further consideration should be paid to the interactions that could occur at the placenta and the blood–cerebrospinal fluid barrier, each of which synthesizes its own TTR for T_4 transport to the fetus and the brain.

"We now know that [EDCs bind] to TTR, so that may mean there is less thyroid hormone transported to critical tissues, like the fetus or to the brain. But it also implies that these compounds that bind to TTR are transported across these barriers," Hamers says. Such open questions are being addressed in ongoing research, including the Assays for the identification of Thyroid Hormone axis-disrupting chemicals: Elaborating Novel Assessment strategies (ATHENA) project,[5] which specifically focuses on thyroid hormone disruptors.

Stapleton notes that what was observed in this study could provide insight into impacts on thyroid regulation at other points downstream of the protein binding. "The thyroid system evolved to be well buffered," she says. The system always tries to counterbalance and get back on the right path if it is perturbed. "But," she adds, "these same chemicals, if they interfere with TTR, could also perturb it at other points on that path. And so you have to worry about the combined effects on development for all these different points."

Julia R. Barrett, MS, ELS, a Madison, WI–based science writer and editor, is a member of the National Association of Science Writers and the Board of Editors in the Life Sciences.

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